Allergy Abstracts

Editor

M. M. ALBERT
Brooklyn, N. Y.

Associate Editors

M. HARTEN
Brooklyn, N. Y.

E. H. WALZER
Bridgeport, Conn.

E. W. KAILIN
Washington, D. C.

R. A. CHAIT
Rockville Center, N. Y.

H. J. FRIEDMAN
Cleveland, Ohio

J. SHERMAN
Baltimore, Md.

B. B. SIEGEL
Far Rockaway, N. Y.

RICHARD WISEMAN
Syracuse, N. Y.

KATHERINE BOWMAN
Brooklyn, N. Y.

Advisory Editor

M. WALZER
Brooklyn, N. Y.

From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 18, Number 3 May, 1953

Asthma and Hay Fever

Sudden Death During Cortisone Therapy of Bronchial Asthma. Jarvinen, K. A. J.: Ann. Int. Med. Fenn. Helsinki **41**: 165, 1952.

A 39-year-old man and a 53-year-old woman died suddenly while under treatment with cortisone for bronchial asthma. The man had received 550 mg. during a six-day period and 75 mg. during a second course of treatment begun after a five-day interval. The woman received a total of 400 mg. of cortisone during four days. In both cases, autopsy findings confirmed the clinical impression of cor pulmonale, pulmonary emphysema, and bronchial asthma. Acute congestion of the gastrointestinal tract was present in both cases. Although the woman had received treatment for only a short time, the adrenals showed pronounced changes. Evidence of acute peripheral circulatory insufficiency was present in both cases. Despite the absence of signs of undesirable effects of cortisone therapy in these 2 cases, the author believes that the possibility that the drug played a part in the fatal outcome cannot be excluded. H.

Contributions of Anesthesiology to the Management of Patients With Asthma. Tausig, D., Papper, E. M., and Barach, A. L.: New York State J. Med. **52**: 1893, 1952.

Over an eleven-year period, 57 asthmatic patients were treated with inhalation ether, 29 with rectal ether, and 20 with intravenous alcohol. The severe cases in status asthmaticus were the ones selected for treatment with ether. Good to excellent results were obtained in 52 per cent of the patients treated with inhalation ether and in 24 per cent of those treated with rectal ether. The discrepancy in results is attributed to the lack of adequate depth of anesthesia from the fixed dose of ether given rectally. The patients treated with inhalation ether were premedicated with atropine or scopolamine and a

barbiturate. When dyspnea and anoxia were marked, preliminary inhalation of 100 per cent oxygen or a helium-oxygen mixture was used with nebulized Vaponefrin until the patient was more comfortable. Ether was then given and the patient gradually taken to plane 3 of stage III anesthesia. Bronchodilatation occurred at this level and the patient was kept there for from thirty to forty-five minutes. At this time, bronchial secretions may be suctioned and bronchoscopy may be performed for suction drainage. In some cases, asthmatic breathing resumed as soon as the anesthesia was lightened. One death, attributed to cardiac failure, occurred following inhalation ether. Less severe asthmatics were treated with intravenous alcohol, and among 20 such cases, 51 per cent experienced good or excellent results. B. S.

The Recognition of Nonallergic Asthma. Unger, L.: Dis. Chest **22**: 671, 1952.

Six cases were admitted to a hospital with mistaken diagnoses of bronchial asthma because of wheezing and dyspnea. Actually, the symptoms in these patients were due to other causes. One patient had a leiomyoma of the trachea; another had a carcinoma of the carina; the third had a substernal goiter; the fourth had silicosis; the fifth had acute cardiac dyspnea (cardiac asthma); and the sixth had bronchiectasis. Eosinophiles in large numbers were found repeatedly in the sputum of the second, fourth, and sixth cases. Only the sixth patient was atopic. E. W.

Grass Pollen in Great Britain. Hyde, H. A.: Acta allergol. **5**: 98, 1952.

Although there are almost 220 species of grass in Great Britain, not more than a dozen are of importance as causes of hay fever over widespread areas. These include sweet vernal, meadow foxtail, timothy, bents, Yorkshire fog, tall catgrass, cockafoot, meadow grasses, perennial rye grass, and several types of fescue. These grasses are largely confined to the lowlands (altitudes below 1,250 feet).

The grass pollen season begins at the end of May. In England and Wales, it lasts until mid-July; in the lowlands of Scotland, it lasts until the beginning of August.

Daily and hourly variations in the pollen content of the air were studied at slide stations in Cardiff and at 8 scattered stations in the lowlands. The actual period during which pollen release takes place may vary with a particular species, but in general pollen release was found to occur mainly in the early morning and late afternoon. The incidence of grass pollination from 1943 to 1950 is reviewed. H.

Therapy of Asthma With Vitamin B_{12}. Caruselli, M.: Riforma med. **66**: 849, 1952.

Good results were obtained with vitamin B_{12} therapy in 10 of 12 patients with bronchial asthma. Vitamin B_{12} was administered orally in doses of 30 mg. for from fifteen to twenty days. Two elderly patients with complicating severe emphysema and hypertensive arteriosclerosis failed to obtain relief with vitamin B_{12}. The author suggests that vitamin B_{12} possesses antiallergic activity. H.

Ventilatory Studies of the Lungs in Asthma. Colldahl, H., and Lundin, G.: Acta allergol. **5**: 37, 1952.

The fall in alveolar nitrogen percentage was used as a measure of the ventilatory efficiency of the lungs during oxygen breathing. The time required for the diminution in alveolar nitrogen down to 2 per cent was used as an index of ventilatory efficiency. In normal patients, the nitrogen washing-out time is

usually 2.5 to 3.0 minutes. Although it may vary, it is more or less constant in the same individual under normal conditions.

Asthma was provoked in patients who were symptom-free by the inhalation of allergenic extracts. The washing-out time was found to be almost doubled by the time the patient experienced the first subjective symptoms of asthma. The objective registering of the washing-out time is considered of particular value for judging the changes occurring after the inhalation of different antigens. The course of the disease has also been studied by this method. H.

Asthma as a Disease of Dysreaction. A New Therapeutic Approach. Salomon, M. I.: New York State J. Med. **52**: 1310, 1952.

Six patients in status asthmaticus were treated with nitrogen mustard intravenously. These patients had not responded to the usual antiasthmatic medications and some had not responded to either ACTH or cortisone. They were injected intravenously with approximately 5 mg. of nitrogen mustard daily for two consecutive days. In 5 of the 6 patients, improvement was marked in from six to twelve hours after the first injection. Adrenalin and aminophylline refractoriness disappeared rapidly. Seven asthmatic patients failed to respond to treatment with triethylene melamine, a derivative of nitrogen mustard, administered by the oral route. B. S.

Dermatology

Attempts at Passive Transfer of Allergic Eczematous Sensitivity in Man by Means of White Cell Suspensions. Baer, R. L., Serri, F., and Kirman, D.: J. Invest. Dermat. **19**: 217, 1952.

White cell suspensions from 66 patients known to have contact sensitivities to various substances were used in attempts to affect passive transfer of the sensitivities. Forty-five cubic centimeters of blood was drawn from each subject and mixed with citrate and fibrinogen and incubated in a water bath at 37° C. The white cells were pipetted off in a plasma suspension before the red cells had completed sedimentation, and then were centrifuged for five minutes at 1,800 R.P.M. A yield of about 0.2 ml. of cells was obtained from each 45 ml. sample of blood. It was suspended in 1 or 2 ml. of plasma and used to sensitize 4 sites on the upper arm of the recipient. The cells were injected into the recipient within forty-five or sixty minutes from the time the blood was drawn from the donor. Most of the 66 substitutes had been previously tested and found to be negative to the specific allergen to which the donor was sensitive, although 16 of the recipients were known to be sensitive to other allergens. The substitutes had various skin disorders, about 80 per cent having either atopic dermatitis or contact dermatitis. No mention was made as to whether their various skin conditions were active at the time the sites were sensitized or tested. After sensitization, the sites were patch-tested at time intervals varying from twelve hours to seventy-two hours, in order to determine the optimum time interval needed to demonstrate passive sensitivity. A control patch was always applied to an unprepared site concomitantly with the application of the patch on the sensitized site. Positive reactions were observed at the cell-injected site and at the control site in 3 recipients (in 1 to paraphenylenediamine, in 1 to mercury bichloride, and in 1 to resorcin). One recipient had a questionably positive reaction to nickel sulfate at both the test and control sites. In 62 recipients, the patch reactions were negative at the injected and control sites. Four of these latter recipients subsequently developed positive reactions to the allergen under study. The authors suggest that the positive reactions were probably due to active sensitization rather than to passive transfer of the sensitivities. The workers, however, consider the possibility that "white cell sus-

pensions of patients with allergic eczematous sensitivities may contain a factor which, when injected intracutaneously into previously non-sensitive subjects, facilitates or stimulates the recipient's specific active sensitization to the allergen to which the donors of the cells are sensitive." R. W.

Failure of a Local Inhibitory Action on Local Injection of the Free Alcohol of Compound F (Hydrocortisone) in Some Dermatologic Lesions. Goldman, L., O'Hara E. H., Emura, E., and Baskett, J.: J. Invest. Dermat. **19**: 267, 1952.

Patients with inflammatory skin lesions such as eczema or psoriasis were injected intracutaneously with the free alcohol of Compound F, Compound F acetate, and cortisone acetate. In contrast to the effects of cortisone and Compound F acetate, the free alcohol of Compound F was found to have no inhibitory influence on inflammatory reactions. When given orally, however, this drug was found to be quite effective in relieving various skin conditions. On intracutaneous injection into normal skin, the free alcohol of Compound F was found to be less irritating than either the acetate of Compound F or cortisone. The free alcohol, like the acetate of Compound F, was found to be ineffective in altering urticarial or histamine wheals. R. W.

Antiallergic Action of Local Anesthetics and Antihistaminics on the Tuberculin Reaction in Man. Lecomte, J.: Acta allergol. **5**: 88, 1952.

Local anesthetics (Novocaine, Percaine, Pantocaine, Xylocaine) and antihistaminics (Neoantergan, Phenergan, Histaphene, Pyribenzamine) when injected simultaneously with tuberculin regularly inhibit the tuberculin reaction in human beings. The author believes that these compounds probably act by suppressing the inflammatory reaction on a nonspecific basis. H.

Exfoliative Dermatitis Due to Banthine. Clark, R. F., and McNaughton, D. W.: Arch. Dermat. & Syph. **66**: 101, 1952.

A 60-year-old white man developed an acute generalized exfoliative dermatitis on the eighth day of treatment with Banthine. The dermatitis improved when the drug was discontinued, became worse when its use was resumed, and improved again after complete withdrawal of the drug. After the skin had cleared, patch tests performed with crushed Banthine tablets elicited positive reactions. Control patch tests made on normal subjects and on other patients taking Banthine gave negative reactions. C.

Neurogenic Factors in Contact Dermatitis. Guy, W. G.: Arch. Dermat. & Syph. **66**: 1, 1952.

In order to demonstrate the effect of nervous and emotional factors in contact dermatitis, guinea pigs previously sensitized to 2-4 dinitrochlorbenzene were subjected for five days to noise and electric shock stimuli severe enough to make them restless, hyperkinetic, decrease their food and water intake, and produce weight loss. After five days of this treatment, the animals showed a tendency to increased skin reactivity as demonstrated by patch test reactions to the 2-4 dinitrochlorbenzene. Ten nonsensitized control animals were subjected to the same shock stimuli for five days and patch-tested with 2-4 dinitrochlorbenzene. Only one showed a positive skin response.

It was concluded that disturbing guinea pigs increased the sensitivity of their skins to contactants. It is inferred that similar environmental influences involving more complex mechanisms and channels might produce the same effects in human beings. C.

The Effect of Topically Applied Compound F in Selected Dermatoses. Sulzberger, M. B., and Witten, V. H.: J. Invest. Dermat. **19**: 101, 1952.

Nineteen patients with long-standing dermatoses who had been refractory to all types of local therapy were given local applications of Compound F (17 hydroxycorticosterone-21-acetate). Patients having involvement of symmetrical sites were chosen so that Compound F ointment could be applied to one area and the ointment base alone to the contralateral area. Improvement following the application of Compound F was noted in 75 per cent of the cases. It occurred during the first week and was maintained as long as the local therapy was continued. No patient was treated for longer than 4 weeks. Improvement was manifested by diminished pruritus and erythema and, in one patient, the beneficial effects extended to sites distant from the actual application of the hormone. R. W.

Experiments on Passive Transfer of Eczematous Allergy. Haxthausen, H.: J. Invest. Dermat. **19**: 293, 1952.

Using a technique similar to that employed by Lawrence for the passive transfer of tuberculin sensitivity by means of suspensions of viable white blood cells, the author attempted the passive transfer of contact sensitivity to specific allergens. Instead of the bovine fibrinogen employed by Lawrence to hasten the sedimentation of white cells from heparinized blood, this worker used a saline gum arabic solution. As a control on this modification in technique, white blood cells were obtained from another blood sample from the same patients by fractionated centrifugation, without the addition of the gum arabic solution. Prior to the intracutaneous injection of 0.1 ml. of the white cell suspension, all recipients were patch tested to rule out possible skin reactivity to the substance to which the donor was sensitive. Patch tests were applied to the experimental sensitive site and to a control site sensitized with white blood cells obtained from a nonsensitive donor. Reactions were read after twenty-four and forty-eight hours. In some instances, intracutaneous tests were performed with soluble allergens. These reactions were read after fifteen and thirty minutes.

Negative patch reactions were obtained in all of the 66 passive transfer tests. The use of gum arabic to hasten sedimentation had no apparent effect on the final results obtained. Four immediate wheal reactions were obtained on sites sensitized with cells from patients sensitive to chromium, mercury, and lucosil; however, only one of the 2 substitutes sensitized with cells from the chromium-sensitive patient showed a positive urticarial reaction. Using the above technique, 9 attempts to transfer tuberculin hypersensitiveness failed. R. W.

Some Immunologic Phenomena in Treatment of and Patch Testing for Ragweed Oil Dermatitis. Fisher, A. A.: J. Invest. Dermat. **19**: 271, 1952.

Eighteen patients with known ragweed oil contact dermatitis were treated orally with ragweed oil. They were given gradually increasing amounts of ragweed oil diluted 1:100, 1:50, and 1:25 in corn oil. The oil was administered in a gelatin capsule which the patients swallowed. They were advised to take the capsule immediately after the morning or evening meal since the oil was best tolerated at that time. During the first week, one drop of the 1:100 dilution was taken daily; during the second week, the dose was two drops daily. If no symptoms of intolerance occurred during the first two weeks, the dosage was increased as rapidly as tolerance permitted until a maintenance dose of 12 drops of the 1:25 dilution was attained. When the maintenance dose was reached, it was necessary to administer it only 2 or 3

times a week. The occurrence of urticaria or a flare-up of the ragweed dermatitis during treatment necessitated a temporary cessation of treatment. Complications of this sort were infrequent when the dosage was increased gradually. Pruritus ani was the most annoying side reaction but usually was controllable by careful cleansing of the anal region.

Most of the patients obtained definite improvement and showed a tendency toward a diminution in their patch reactions. In 4 patients under treatment for five years, the previously positive patch reactions were either completely or almost completely abolished. The dye used to color the ragweed oil oleoresin was found to be a potent nonspecific reactor, especially in those patients sensitive to paraphenylenediamine. The author advises, therefore, that all ragweed oleoresin used for patch testing should have no added coloring matter.

All 18 cases of ragweed dermatitis were given patch tests with cocklebur, sheep sorrel, hickory, buck horn, Kentucky bluegrass, red top, poison ivy, orchard grass, timothy, oak, chrysanthemum, pyrethrum, and turpentine. Eight of the 18 patients reacted to poison ivy, 6 reacted to turpentine, 4 to cocklebur, 4 to chrysanthemum, and all of the 18 reacted strongly to pyrethrum. However, only 3 of 8 cases of pyrethrum dermatitis gave positive reactions to ragweed oleoresin. On the basis of this finding, the author now adds pyrethrum to the treatment material for oral administration to most patients who have ragweed dermatitis. R. W.

Experimental Histamine Pruritus. 1. Influence of Physical and Psychological Factors on Threshold Reactivity. Cormia, F. E.: J. Invest. Dermat. **19**: 21, 1952.

Sixty-nine patients, 39 of whom were either control subjects or had dermatoses not markedly influenced by psychogenic factors, were tested intracutaneously with 0.05 ml. of histamine in dilutions ranging from 1:1,000 to 1:10,000,000. Injections were usually made on the forearm except when the location of the dermatitis made this impractical. It was found that the subjective reaction to histamine usually paralleled the objective one and that the younger the individual the more likely he was to obtain a subjective reaction. Buffered saline dilutions of histamine were found to cause less burning and irritation than dilutions made with normal saline. In patients with severe clinical pruritus, the itch often extended well beyond the area of the flare, and stroking the skin lightly in the flare area either produced itching or caused it to return if it had already subsided. Patients experiencing the greatest amount of pruritus clinically responded to the weaker dilutions of histamine. Itch thresholds to histamine in involved skin were always much lower than those in normal skin. Even in the absence of visible inflammation, the itch threshold was extremely low in areas of acute severe dermatitis or psychogenic pruritus. ACTH failed to influence responses on uninvolved skin. Patients with psychogenic dermatoses were found to have a much lower itch threshold when placed under emotional stress, but this threshold could be quickly raised when the patient was given reassurance. Neither Mecholyl nor banthine influenced the histamine itch threshold response, suggesting that the liberation of acetylcholine is not the factor responsible for lowering the itch threshold following psychic trauma. R. W.

Effect of Cortisone and Adrenocorticotropic Hormone on Delayed Hypersensitivity to 2,4-Dinitrochlorobenzene in Guinea Pigs. Jeter, W. S., and Seebohm, P. M.: Proc. Soc. Exper. Biol. & Med. **80**: 694, 1952.

Guinea pigs were sensitized with 2,4-dinitrochlorobenzene by daily applications of the chemical to the skin for one week. One week following the

last application, the animals were patch tested with the chemical and the skin reactions were read at twenty-four and forty-eight hours. Groups of the sensitized guinea pigs were treated with varying doses of cortisone on ACTH for forty-eight hours prior to the skin test. The skin sensitivity of the hormone-treated group did not differ from that of the control group. Treatment with cortisone or ACTH during the course of the sensitization process also failed to affect the skin reactivity. B. S.

Dermatitis Venenata Due to Potassium Undecylenate. Rogers, S. I., and Shatin, H.: Arch. Dermat. & Syph. **66**: 289, 1952.

A 52-year-old white man with athlete's foot developed typical lesions of dermatitis venenata after 2 applications to the feet of Timofax ointment, a cream containing 10 per cent undecylenic acid as free acid and potassium salt.

Marked positive reactions were obtained on patch testing with Timofax ointment and powder, both of which contained undecylenic acid, methyl salicylate, eucalyptus oil, and potassium undecylenate. Of these compounds, only potassium undecylenate powder yielded a positive patch reaction. Control subjects patch tested with potassium undecylenate powder showed no reactions. Sensitization to potassium undecylenate and to other undecylenic acid salts is very rare. C.

On Hypersensitivity to the "Para Group." Rajka, G.: Acta allergol. **5**: 11, 1952.

Hypersensitivity to the "para group" as an example of positional isomery and the relationship of chemical structure to sensitization is reviewed.

Twenty-three patients sensitized to the "para group" were patch tested with various substances. A wide range of individual differences was found. Although patients might show hypersensitivity to any of the compounds belonging to this group, it was impossible to predict which substances in the group would yield positive reactions on any particular patient. The difficulties encountered in studying the relationship of chemical structure to sensitization by means of patch test studies with various similar compounds are demonstrated.

The author cites the case of a woman sensitized to paraphenylenediamine, nylon dye, and other substances of the "para group" who repeatedly developed new skin lesions following the ingestion of acid yellow or amaranth. Both these substances are azodyes used to color foods in Hungary.

Dyes, especially those encountered by hairdressers and textile dyers, frequently are primary sensitizers to the para group. Procaine, especially in ointments, is a common sensitizing agent.

All patients who react with allergic symptoms to any of the sulfonamides, PAS, p-aminobenzoic acid, procaine (pontocaine, benzocaine), and other drugs of para (para-amino-) structure should, where possible, be treated with substitute drugs of different chemical structure. H.

Otorhinology and Ophthalmology

Conjunctivitis as Sole Manifestation of Delayed Reaction to Pollen Antigens. Diamond, H. E.: New York State J. Med. **52**: 1564, 1952.

A 45-year-old man with bronchial asthma, vasomotor rhinitis, and chronic sinusitis was treated for several years on a perennial basis with ragweed, timothy, plantain, and house dust extracts. He began to notice a dull pain in the eyes and reddening of the conjunctivae about twenty-four hours

after each pollen injection. The conjunctivitis cleared rapidly following the administration of an antihistaminic drug. When the pollen dosage was reduced to about half of the previous level, there were no further eye symptoms. B. S.

Miscellaneous Allergies

Denatured Insulin: A Simplified, Rapid Means of Treatment of Allergy to Insulin Complicating Diabetic Ketosis. Dolger, H.: New York State J. Med. **52**: 2026, 1952.

Four patients with constitutional allergic reactions and 6 patients with fairly severe local cutaneous reactions were successfully treated with denatured insulin. In patients with diabetic ketosis and constitutional allergic reactions to insulin, the use of denatured insulin was found to be preferable to rapid desensitization, since it offered a simpler and faster means of supplying urgently needed insulin. The insulin was denatured by immersing the vial in boiling water for thirty minutes. It had been found that regular and crystalline zinc insulin can withstand boiling for three hours and retain more than one-half of its physiologic activity. Denaturing by heat is not applicable to the modified types, such as protamine zinc, globin, and N P H insulin. In the patients with generalized allergic reactions, treatment with denatured insulin was continued for two or three weeks. Any type of commercially available insulin could then be substituted without difficulty. Immunologic studies with denatured insulin were not done. B. S.

Allergic Reactions to Para-Aminosalicylic Acid. Report of Seven Cases, Including One Case of Loeffler's Syndrome. Warring, F. C., and Howlett, K. S.: Am. Rev. Tuberc. **65**: 235, 1952.

Hypersensitivity to para-aminosalicylic acid was observed in 7 tuberculous patients who were receiving the drug in conjunction with streptomycin. This represented an incidence of approximately 2.5 per cent of those who were receiving PAS at a large sanatorium. A past history of atopic disease was elicited in 3 patients. Symptoms encountered included fever, chills, urticaria, other rashes, headache, nausea, vomiting, diarrhea, coryza, sneezing, tearing, conjunctivitis, coughing, wheezing, malaise, and lymphadenopathy. Blood eosinophile counts above 5 per cent were noted in 3 of the patients. Successful oral desensitization to PAS was accomplished in 4 patients and the drug was tolerated thereafter in therapeutic doses. In one patient, an acute transitory patchy pneumonitis with sputum and blood eosinophilia occurred after each of 3 attempts to institute PAS therapy. After a "desensitizing" regime, this patient was able to tolerate therapeutic doses of the medication. E. W.

Anaphylaxis

Histamine Shock and Vitamins. Naranjo, P.: Proc. Soc. Exper. Biol. & Med. **81**: 111, 1952.

The time elapsing between the administration of histamine aerosol and the onset of symptoms of shock was determined in a group of guinea pigs. Part of this group were then pretreated with a number of vitamins and the experiment was repeated. It was found that vitamins B_{12}, C, B, G complex, and K, in small or large doses, afforded no protection against histamine shock. It was also found that the fall of blood pressure produced by the intravenous injection of histamine in cats and guinea pigs was not prevented by a prior intravenous injection of vitamin B_{12}. Furthermore, varied doses of vitamins B_{12} and C were found to be ineffective in preventing histamine contractions of excised guinea pig ileum. The results of these experiments are in contrast to those obtained by previous workers. B. S.

Anaphylactic Shock in the Pertussis Vaccinated Mouse. II. Diphtheria and Tetanus Toxoids as Antigens. Malkiel, S., and Hargis, B. J.: Proc. Soc. Exper. Biol. & Med. **81**: 109, 1952.

White mice were injected intraperitoneally with a mixture of *H. pertussis* vaccine and fluid diphtheria toxoid, alum-precipitated diphtheria toxoid, fluid tetanus toxoid, or alum-precipitated tetanus toxoid. Control groups of mice received only diphtheria toxoid. Fifteen days after sensitization the mice were injected intravenously with the respective toxoid. The anaphylactogenicity of the antigens was determined by the mortality rate after the challenging injection. The mortality rate was computed on the basis of the percentage of animals dead after twenty-four hours. It was found that the *H. pertussis* vaccine markedly enhanced the anaphylactogenicity of the diphtheria toxoids, but had no effect on the tetanus toxoids. When the experiment was repeated using a ten-day instead of a fifteen-day incubating period, similar results were obtained. B. S.

Pharmacology, Physiology, and Pathology

The Effects of Cortisone on the Cutaneous Histamine Response of Rabbits Using Evans Blue Dye as an Indicator. Chappell, J. W., Ebert, R. H., and Barclay, W. R.: J. Lab. & Clin. Med. **39**: 896, 1952.

The effects of cortisone on the cutaneous histamine response of rabbits, using Evans blue dye as an indicator, were tested 44 times in a total of 30 rabbits. Testing solutions of histamine phosphate varied in concentration from 0.01 mg. to 1.0 mg. per ml. of free base. Immediately following the intracutaneous introduction of histamine, the rabbits were injected intravenously with Evans blue solution. Treated animals received 10 mg. doses of cortisone per day for varying periods of time prior to the histamine test. In each experiment, the results were controlled by comparison of the responses of cortisone-treated animals with those of untreated animals. The response in untreated animals consisted of a blue halo which appeared within a few minutes in the margin of histamine injection blebs and grew peripherally, reaching full development within thirty minutes. Within the halos, the blebs showed early pallor which was later replaced by staining. It was noted that the stronger the solution of histamine employed, the darker the halo. In 75 per cent of cortisone-treated animals, there was no staining; in the remainder there was poor staining. This inhibition of staining was noted in all cortisone-treated animals which had received as little as 2 doses of hormone. That this inhibition of staining was not due to effects of electrolyte changes or altered plasma was demonstrated in other experiments. In these experiments, large doses of dye were given to rabbits which had received large doses of cortisone. When plasma from these animals was given to untreated animals, there was no inhibition of staining. It was concluded that cortisone administration produced marked inhibition of the cutaneous histamine response of rabbits as measured by diffusion of Evans blue dye. This effect was shown to be due to the action affecting capillary permeability rather than to retention of dye by altered serum. E. W.

The Renal Excretion of Histamine and Histidine in Man, and the Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone Administration. Grob, D.: Bull. Johns Hopkins Hosp. **90**: 341, 1952.

The metabolism of histamine and histidine, two closely related chemical compounds, was studied in allergic patients, in individuals suffering from chronic ailments, and in normal controls. It was found that the average

normal daily excretion of histamine was 8 mg. in twenty-four hours while that of histidine was 68 mg. in twenty-four hours. Patients suffering from bronchial asthma, lupus erythematosus, rheumatoid arthritis, and myasthenia gravis showed essentially the same blood and urinary excretion levels as the controls. The serum concentration of histidine and the urinary excretion of histamine and histidine bore no relation to the occurrence of asthmatic paroxysms or urticarial attacks. The concentration of histidine in transudates and exudates was about the same as that found in the serum. Due to the extremely low serum concentrations of histamine, it was impossible to study the mechanism of renal excretion of this compound. Injected histidine, however, was found to disappear from extracellular fluids much more rapidly than it could possibly be excreted by the kidneys, indicating that it is removed from extracellular fluid by other than renal mechanisms. While there was only a transient increase in histamine excretion following ACTH or cortisone therapy in patients with allergic diseases of myasthenia gravis, there was a marked sustained increase in histidine excretion. Following cessation of the hormone therapy, the histidine excretion rate quickly returned to normal within two to six days. Although patients with allergic conditions were usually benefited by adrenal cortical stimulation and those with myasthenia gravis were not, histamine and histidine excretion in the two conditions was similar. Detectable histamine blood cell content was not influenced by ACTH or cortisone. The increased excretion of histidine seemed to result from decreased tubular reabsorption. Following hormone therapy, the extrarenal uptake of histidine from extracellular fluid was diminished. It is suggested that the latter effect as well as the decrease in tubular reabsorption may be the result of a widespread decrease in cellular transport and utilization of histidine. R. W.

Nephrotoxic Globulin Nephritis. 1. Course After a Single Injection. Lippman, R. W., Marti, H. U., and Campbell, D. H.: Arch. Path. **53**: 1, 1952.

Anti-rat-kidney rabbit serum was prepared for four months with a suspension of rat kidney tissue. The antibody globulin was precipitated from the blood serum and was found to consist entirely of gamma globulin.

Groups of female rats were given single intravenous injections of the serum and one group was sacrificed at each of the following intervals: thirty minutes, two hours, four hours, six hours, twenty-four hours, one week, four weeks, and four months. Several groups of rats were injected with globulin from a control serum and similarly sacrificed.

A detailed description is given of the renal lesions encountered in the different groups of animals. The lesions observed indicated a progressive development of a mild proliferative glomerulonephritis with moderate tubular degeneration. The first signs were noted as early as thirty minutes after administration of the nephrotoxic serum, and maximum evidence of damage occurred at one week. Thereafter, the lesions receded with evidence of repair. The control animals showed no significant changes.

It was shown that the nephrotoxic activity of anti-rat-kidney rabbit serum resided wholly in the gamma globulin fraction. J. S.

A Simple Method for the Determination of Vital Capacity-Time Relationships. Segal, M. S., Herschfus, J. A., and Dulfano, M. J.: Dis. Chest **22**: 123, 1952.

A simple ruler-graph device is described for use with single determinations of vital capacity on a recording drum apparatus. This permits the

rapid determination of the volume of air ejected during each second of the vital capacity tracing on a graphic record. The results obtained on this apparatus when patients were relieved of bronchospasm by the administration of certain medications were compared with those obtained on the vitalometer. Both methods yielded comparative values. The apparatus herein described, however, yielded additional significant data. E. W.

Studies on Hypersensitivity Arteritis in Rabbits. 1. Effect of Acute Arteritis on Blood Pressure. 2. Observations on Animals Subjected to Numerous Large Injections of Horse Serum. Orbison, J. L.: Arch. Path. **53**: 352, 1952.

The effect on blood pressure of experimentally produced hypersensitivity arteritis in rabbits was investigated. Groups of animals were injected intravenously with horse serum. Long- and short-term experiments, varying from one to seven months, were performed. Blood pressure determinations were made in the central artery of the ear. No significant elevation of blood pressure was observed in the rabbits in any of the experiments.

At autopsy, acute necrotizing and inflammatory lesions were noted in the short-term experiments. In the long-term experiments, where the animals received repeated injections of large amounts of horse serum over several months, only few arterial lesions were noted, and these were in various stages of healing. Endocardial lesions were prominent in all animals in both short- and long-term experiments. This suggested that the arteries of the animals became less reactive to the antigen with repeated injections, but the reactivity of the endocardium remained unaltered.

The lesions of the heart, liver, and kidneys were similar to those previously reported. Glomerular lesions were not observed in the kidneys. The absence of these lesions in these animals could not be explained. J. S.

Miscellaneous

Suppression of the Shwartzman Phenomenon by Adrenocorticotropic Hormone and Cortisone: Quantitative Aspects. Marcus, S., and Donaldson, D. M.: J. Immunol. **69**: 101, 1952.

Bacterial filtrates were prepared from *Salmonella aertrycke* by centrifuging the cultures, decanting the supernatant, and adding formalin as a preservative. The filtrates were tested for sterility and for their ability to induce Shwartzman reactions prior to studying the effect of ACTH or cortisone on the phenomenon. Rabbits were given 4 preparatory intradermal injections. ACTH was injected subcutaneously in divided doses of varying amounts prior to and following the preparatory and provocative injections or just prior to and after the intravenous injection. Cortisone was administered intramuscularly on a dosage and time schedule similar to that followed for ACTH. Control groups received neither ACTH nor cortisone. The intradermally prepared site manifested less edema and the diameter of reaction was less when injections of hormone were begun prior to the preparatory intradermal injection. When injections were begun prior to the intradermal challenge and continued throughout the experiment, small petechiae developed at the intradermally injected skin sites at the time of the intravenous injection. A definite relationship was found to exist between the inhibition of the inflammatory reaction obtained six hours following the intravenous injection and the type, amount, and time of hormone therapy. The necrotic reaction was the most easily preventable response, while the edematous reaction was

least affected by hormone therapy. Cortisone never produced significant diminution in reddening, whereas ACTH therapy always affected the amount of reddening obtained. If hormone injections were not given prior to the preparatory injection, minimal inhibition was observed in the final reaction. Twenty-nine per cent of ACTH-treated animals, 4 per cent of the cortisone-treated rabbits, and 18 per cent of the control animals died within twenty-four hours after the intravenous injection of bacterial filtrate. It appears, therefore, that cortisone inhibits both the skin and systemic response of the intravenously injected bacterial filtrate, whereas ACTH inhibits the skin response but makes the animal concomitantly more susceptible to the generalized toxic effect of the bacterial filtrate. R. W.

Effect of Various Allergens and Antibiotics on Experimental Poliomyelitis. Milzer, A., and Nicholson, F.: Proc. Soc. Exper. Biol. & Med. **80**: 442, 1952.

Mice were inoculated intracerebrally with approximately 10 LD_{50} units of the Lansing strain of poliomyelitis virus. On the first, third, and fifth days after virus inoculation, the mice were injected intravenously or intraperitoneally with one of the following allergenic extracts: house dust, mixed tree pollen, mixed grass pollen, ragweed pollen, or mixed mold spore extract; horse serum: dihydrostreptomycin; terramycin; penicillin; or *Salmonella typhimurium* vaccine. Control mice were injected with nutrient broth after the same intervals. There was no significant reduction in the average incubation period before onset of paralysis in all experiments in which mice were injected with the various allergens, antibiotics, or nutrient broth. However, the Salmonella vaccine produced a consistent reduction in the incubation period before the onset of paralysis. In previous experiments, the inoculation of pertussis vaccine and pertussis-diphtheria toxoid were also found capable of significantly decreasing the incubation period before the onset of paralysis. B. S.

Passive Immunity to Vaccinia in Newborns. II. Response to Vaccinations. Kempe, C. H.: Yale J. Biol. & Med. **24**: 331, 1952.

Two infants with high hemagglutination-inhibition antibody titers in the cord blood failed to show any skin reaction when vaccinated on the fifth day of life. This failure to "take" occurred after each of 3 attempts at vaccination. Two infants with low antibody titers who were vaccinated on the fifth day of life had a "vaccination take" which was maximum in ten days. At approximately 6 months of age, repeat vaccinations of 3 of the 4 infants were performed. Two of these infants, who had a titer of 1:160 and 1:40 prior to this vaccination, produced no early allergic or immune response. These infants developed a maximal reaction on the fifth and sixth days, respectively. The other infant, who had a "take" with the initial vaccination and a titer of only 1:10, had an early sensitivity response which resulted in a typical vaccinoid reaction maximal on the sixth day. The absence of an early sensitivity reaction in the infants with high prevaccination titers indicated the lack of a previous antigenic exposure to the virus. It was suggested that these were modified primary "vaccinia takes." Revaccination of these children at 1 year of age resulted in a sensitivity type or immune early reaction maximal on the second day after vaccination. E. W.